REMARKS

Applicants respectfully request reconsideration and withdrawal of the outstanding Office Action rejections in view of the following remarks. Applicants would like to express gratitude to the Examiner for indicating present claims 1-17, 21-30, and 32 as allowable.

Response to Claim Rejections under 35 U.S.C. §112

Claims 18-20 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner asserts that the function of the second peptide or polypeptide immune response of claim 18 is not clear. Applicants respectfully disagree.

Applicants submit that a bacterial cell, as defined in claim 18, is based on the teaching on page 7, lines 26-36 of the specification which states that the recombinant bacterial cell may contain further immunogenic peptides or polypeptides to elicit an immune response. For example, the peptide of polypeptide may be selected from Mycobacterium antigens or, in a wider sense, from autoantigens, tumor antigens, pathogen antigens and immunogenic fragments thereof. Further specific examples of such immunogenic peptides or polypeptides can be found in the paragraph bridging pages 4 and 5 of the specification. The combination of the expression of at least a second protein in the bacterial cell together with the advantages of the cell (urease-deficiency and the expression of a phagolysosomal escape protein) would lead to an improved immune response against the at least one second protein.

Further, the application discloses that the immune response elicited by the immunogenic protein can be a B cell-mediated immune response or, preferably, a T

cell-mediated immune response (see page 5, lines 18-22 of the specification). Accordingly, it would have been clear to one of ordinary skill in the art that the immune response to be elicited by the at least one second recombinant nucleic acid would have been determined by the identity of the peptide or polypeptide encoded by the recombinant nucleic acid(s).

Applicants respectfully request withdrawal of the rejection of claim 18 under 35 U.S.C. §112, second paragraph, for the above reasons and because there is clear disclosure of definitive immunogenic functions of the claimed second peptide or polypeptide in the specification. Claims 19-20, depending from claim 18, should be allowable for at least the reasons above. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112 and that claims 18-20 be allowed.

Claim 31 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for the same reason as above. Applicants submit that the method of claim 31, namely inserting at least one second recombinant nucleic acid molecule into the bacterial cell, said second recombinant nucleic acid molecule encoding a peptide or polypeptide capable of eliciting an immune response in a mammal, would have been clear to one of skill in the art because inserting a second peptide or polypeptide to elicit a desired immune response is clearly and definitively described in the specification as mentioned in the preceding paragraphs. Thus, Applicants respectfully request withdrawal of the rejection of claim 31 under 35 U.S.C. §112, second paragraph, for the above reasons and the clear disclosure of definitive immunogenic functions of the claimed second peptide or polypeptide in the specification.

Claims 39-46 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner asserts that the specification teaches treatment of mice or guinea pigs infected with *M. tuberculosis* or *M. bovis* BCG, but does not convey to those skilled in the art that the inventors had possession of the claimed method for treating any mammal having any disease state.

Applicants submit that there is a clear description in the Examples of using the claimed method to treat mice and guinea pigs, i.e., mammals, infected with *M. tuberculosis* and *M. bovis* BCG, i.e. disease states. These animal models are well-known models for the development, testing, and confirmation of therapeutic compositions and methods for treating humans and other mammals. In the absence of evidence to the contrary, Applicants submit that the positive results in well-known animal models reasonably convey to those skilled in the art that the inventors did have possession of the invention at the time of filing.

Applicants submit that claim 40, directed to treating a mammal with tuberculosis is clearly described in the specification and examples, especially Example 3. Applicants respectfully request withdrawal of the outstanding rejection of claim 40 based on the above arguments.

Further, with regard to claim 41, there is written description of using the claimed method in immunodeficient mammals, at least in Example 3. Also, with regard to a mammal having a HIV disease state as recited in claim 42, a mammal having a tumor as recited in claim 43, and a superficial bladder cancer disease state as recited in claim 44, there is disclosure on page 9, lines 11-23 that states:

> Due to the high safety of urease-deficient bacterial cells, which was demonstrated in two different animal models (Example 3), the living vaccine of the present invention is particularly suitable for administration to immunodeficient subjects, e.g. subjects suffering from an HIV infection or subjects which are treated with immunosuppressive drugs. In an especially preferred embodiment, the living vaccine of the present invention is used as a tuberculosis vaccine for immunodeficient subjects.
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> In a further preferred embodiment, the living vaccine is used as a tumor vaccine, e.g. as a vaccine against superficial bladder cancer. In a still further preferred embodiment of the invention, the living vaccine is used in the veterinary field, e.g. as a vaccine against listeriosis, paratuberculosis or bovine tuberculosis.

Thus, the specification does indeed provide a written description of using the claimed method to treat immunodeficient mammals including those with *M. tuberculosis* and *M. bovis* BCG infections, HIV, tumors, and superficial bladder cancer, i.e. disease states.

Applicants respectfully request withdrawal of the rejection of claim 39 under 35 U.S.C. §112, first paragraph, for the above reasons and the clear disclosure and examples of treating representative mammals suffering from disease states. Claims 40-46, depending from claim 39, should be allowable for at least the reasons above. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112 and that claims 39-46 be allowed.

Conclusions

In view of the foregoing amendment and remarks presented herein, all of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner

reconsider all presently outstanding objections and rejections, and that they be withdrawn. Early and favorable action is awaited.

Applicant believes that a full and complete reply has been made to the outstanding Office Action and a Notice of Allowance is respectfully solicited.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

If any extension of time is required in connection with the filing of this paper and has not been requested separately, such extension is hereby requested.

The Commissioner is hereby authorized to charge any fees and to credit any overpayments that may be required with respect to this paper to Counsel's Deposit Account No.02-2135.

Respectfully submitted,

By

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